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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/726,615	12/04/2003	Vivek M. Rangnekar	104072.B000118	5759
23911 7590 08/20/2009 CROWELL & MORING LLP INTELLECTUAL PROPERTY GROUP P.O. BOX 14300 WASHINGTON, DC 20044-4300				
EXAMINER				
MARVICH, MARIA				
ART UNIT		PAPER NUMBER		
1633				
MAIL DATE		DELIVERY MODE		
08/20/2009		PAPER		

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

### Office Action Summary

**Application No.**

10/726,615

**Applicant(s)**

RANGNEKAR, VIVEK M.

**Examiner**

MARIA B. MARVICH

**Art Unit**

1633

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --  
**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 27 April 2009.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 1, 6-8, 10, 11 and 18-24 is/are pending in the application.
- 4a) Of the above claim(s) 8, 10, 11 and 18-23 is/are withdrawn from consideration.
- 5) ☒ Claim(s) 1 and 6 is/are allowed.
- 6) ☒ Claim(s) 7 and 24 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 04 December 2003 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO/SB/08)  
Paper No(s)/Mail Date \_\_\_\_\_
- 4) ☐ Interview Summary (PTO-413)  
Paper No(s)/Mail Date \_\_\_\_\_
- 5) ☐ Notice of Informal Patent Application
- 6) ☐ Other: \_\_\_\_\_

### DETAILED ACTION

This office action is in response to an amendment filed 4/27/09. Claims 1, 6-8, 10, 11 and 18-24 are pending.

#### *Election/Restrictions*

Claims 1 and 6 are directed to an allowable product. Pursuant to the procedures set forth in MPEP § 821.04(B), claim 7, directed to the process of making or using an allowable product, previously withdrawn from consideration as a result of a restriction requirement, is hereby rejoined and fully examined for patentability under 37 CFR 1.104.

Because all claims previously withdrawn from consideration under 37 CFR 1.142 have been rejoined, **the restriction requirement as set forth in the Office action mailed on 10/6/06 as pertains to claim 7 is hereby withdrawn.** In view of the withdrawal of the restriction requirement as to the rejoined inventions, applicant(s) are advised that if any claim presented in a continuation or divisional application is anticipated by, or includes all the limitations of, a claim that is allowable in the present application, such claim may be subject to provisional statutory and/or nonstatutory double patenting rejections over the claims of the instant application. Once the restriction requirement is withdrawn, the provisions of 35 U.S.C. 121 are no longer applicable. See *In re Ziegler*, 443 F.2d 1211, 1215, 170 USPQ 129, 131-32 (CCPA 1971). See also MPEP § 804.01.

Claims 8, 10, 11 and 18-23 are withdrawn. Therefore, claims 1, 6, 7 and 24 are under examination in this application.

***Claim Rejections - 35 USC § 112, first paragraph***

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 7 and 24 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claim 24 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

**This is a new rejection.**

Claim 24 is drawn to a pharmaceutical composition comprising a *modified* PAR-4 protein fragment selected from the group consisting of 1-204, 137-221, 137-213, 137-198 and 137-195 of rat PAR-4. Hence, the polypeptide is not just PAR-4 fragment but is a modified PAR-4 fragment wherein the modified Par-4 is effective in reducing the size of tumors resistant to Par-4. A modification can be any of a variety of modifications such as insertions, substitutions, deletions, modified nucleic acids resulting in a broad and diverse genus of peptides. However, the efficacy of the peptide is based upon its pro-apoptotic activity in cancer cells, which is described as the result of deletion of sequences outside of the critical "death domain". Applicants

do not teach any modified Par-4 fragments nor do applicants provide structural requirements other than the core domain such that a person of skill in the art would know what amino acids can be substituted in any Par-4 protein. Hence, it would require undue experimentation to determine those amino acids in the Par-4 protein fragment that can be modified and still lead to reduction of tumor size of Par-4 resistant tumors given the lack of guidance in the specification.

The written description requirement under 35 USC 112, first paragraph may be met by sufficient description of a representative number of species by actual reduction to practice, reduction to drawings, or by disclosure of relevant identifying characteristics, i.e. structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between structure and function, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the claimed genus.

Applicant is referred to the Guidelines on Written Description published at FR 66(4) 1099-1111 (January 5, 2001) (also available at [www.uspto.gov](http://www.uspto.gov)). In this case, the nomenclature 1-204, 137-221, 137-213, 137-198 and 137-195 translates into peptides that have been deleted of all but a core region applicants have identified as a death domain in rat protein. Hence, rat Par-4 comprises a unique core domain that is 59 amino acids that comprises a nuclear localization domain and two phosphorylation sites that are localized to between position 137 and 195 of “the wild-type rat Par-4” protein. This region contains a nuclear localization sequence, which is sufficient and necessary to induce apoptosis in Par-4 resistant cancer cells as well as Gas pro death pathway activation. Par-4 mutants deleted of the nuclear localization signal at 147-153 did not enter the nucleus and did not lead to apoptosis of PC3 cells. And Par-4 mutants 1-204, 137-221, 137-213, 137-198 and 137-195 lead to apoptosis in transient transfections in several cancer

cells but not the corresponding normal cells. A panel of androgen dependent or independent prostate cancer cells, immortalized cells and primary cells were tested. Apoptosis was induced in androgen dependent and independent cells but not the normal or immortalized cells (see Table 1 and 2).

Given the unknown size and nature of the recited modifications and the inability to determine if there are modifications that also possess the ability to encode a death domain within the exact recited amino acids, it is concluded that the invention must be empirically determined. In an unpredictable art, the disclosure of full length and JNK binding fragments would not represent to the skilled artisan a representative number of species sufficient to show applicants were in possession of claimed genus.

Claim 7 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter, which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. **This is a new rejection necessitated by applicants' amendment.**

The test of enablement is whether one skilled in the art could make and use the claimed invention from the disclosures in the patent coupled with information known in the art without undue experimentation (United States v. Teletronics, Inc., 8 USPQ2d 1217 (Fed. Cir. 1988)). whether undue experimentation is required is not based on a single factor but is rather a conclusion reached by weighing many factors (See Exparte. Forman, 230 USPQ 546 (Bd. Pat.

App. & Inter, 1986) and In re Wands, 8USPQ2d 1400 (Fed. Cir. 1988); these factors include the following:

The claims are drawn to a Par-4 fragment effective in reducing the size of tumors resistant to Par-4. Claims 7 is drawn to a method of producing the PAR-4 polypeptides by incubating a cell comprising a nucleic acid encoding the PAR-4 polypeptide under conditions that allow expression of the peptide. However, the nucleic acid cannot express the coding sequences regardless of the conditions absent an expression control sequence or promoter sequence operably attached to the coding sequences. Given the unpredictability of performing the invention absent such sequences, a person of skill in the art would have to conduct undue experimentation to practice the claimed invention.

### ***Conclusion***

Any inquiry concerning this communication or earlier communications from the examiner should be directed to MARIA B. MARVICH whose telephone number is (571)272-0774. The examiner can normally be reached on M-F (7:00-4:00).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph Woitach, PhD can be reached on (571)-272-0739. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Maria B Marvich, PhD  
Examiner  
Art Unit 1633

/Maria B Marvich/  
Primary Examiner, Art Unit 1633